

Atty. Dkt. No. 026063-1402

REMARKS

The claims of the present invention concern labeled dideoxynucleotides useful as dye terminators in sequencing reactions, in which a dye is attached to the dideoxynucleotide via a linker at least 10 atoms in length, and kits including such compounds.

Sequence Rules

The Examiner stated that the application does not comply with the requirements of 37 CFR 1.821-1.825, stating there was no CRF and that the sequence in Figure 1 is not in the sequence listing. Applicant requests that the CRF from the parent application 09/018,695 be utilized in the present application. In connection with Figure 1, the nucleotides in that figure show correspondence of specific nucleotides with peaks in the fluorescent graph. As such, the figure primarily shows that correspondence. Thus, the Figure 1 information should not be required to be included in the Sequence Listing.

However, if the Examiner continues to believe that the Figure 1 information must be included in the Sequence Listing, Applicant will submit a new Sequence Listing and CRF. Applicant requests that the Examiner notify the undersigned by telephone if such new Sequence Listing is required.

Rejections under 35 USC §102

The Examiner rejected claims 1-13 under 35 USC §102(b) as allegedly being anticipated by Kumar, WO 99/40223. Applicant requests that the Examiner note that the cited reference is a PCT application claiming priority to US application 09/018,695, which is the parent to the present application. Therefore, the cited application is not prior art to this application. Applicant respectfully requests that the Examiner reconsider and withdraw this rejection.

Rejections under 35 USC §103

The Examiner rejected claims 3 and 9 over Evangelista et al., *Anal. Biochem.* (1996) 235:89-97, and rejected claims 1-3 and 9 over Evangelista et al. in view of Tabor et al., US Patent 5,614,365, and rejected claims 3, 4, and 9 over Evangelista in view of Haralambidis et al., *Nucl. Acids Research* (1987) 15(12):4857-4876. The Examiner asserted that it would have been

Atty. Dkt. No. 026063-1402

prima facie obvious to modify the labeled deoxynucleotide triphosphates of Evangelista into dideoxynucleotides. Applicant respectfully traverses these rejections.

The reference central to these rejections is Evangelista et al. Applicant respectfully submits that it would not have been obvious to use labeled dideoxynucleotides instead of the labeled deoxynucleotide triphosphates described in Evangelista.

First, the use of labeled dideoxynucleotides in the applications described in Evangelista would not be functional. Evangelista described gap-filling and the like. The present compounds act as terminators, so that insertion of the dideoxynucleotides would terminate the synthesis, preventing completion of gap filling. The mere mention in Evangelista of the use of dideoxynucleotides for a different purpose does not suggest use of dideoxynucleotides with the dyes and linkers as specified for sequencing. Thus, Evangelista cannot suggest the present invention.

In addition it is known that even though the various deoxynucleotides are incorporated by a variety of DNA polymerases relatively uniformly, the lack of uniformity of dideoxynucleotides and the resulting uneven signals for sequences terminated with different dideoxynucleotides is a significant problem. No of the references cited by the Examiner indicate that use of dideoxynucleotides with attached linker and dye would not simply exacerbate the problem. Thus, for example, the incorporation of the deoxynucleotides described in Evangelista provides no suggestion, and thus no motivation, that dideoxynucleotides with attached linker and dye would provide improved band uniformity and resolution of band compression artifacts. Likewise, none of the other references cited by the Examiner provide the requisite suggestion.

Indeed, contrary to the Examiner's assertion, there is no suggestion or motivation to combine the references. In view of lack of suggestion by Evangelista, as discussed above, to use the present dideoxynucleotides with attached linker and dye in sequencing, there is no suggestion or motivation to combine Evangelista with either Tabor or Haralambidis. The requirement for such suggestion is well-established by the Federal Circuit. In addition, the Examiner must provide a clear showing supported by evidence of such suggestion. In the present case, Applicant submits that such a clear showing is not made, so that a prima facie case of obviousness is not made.

Thus, in view of the lack of suggestion from Evangelista to use dideoxynucleotides with attached linker and dye as described for the present invention, Applicant respectfully submits

Atty. Dkt. No. 026063-1402

that a prima facie case of obviousness in not made. In addition, even if the references were combined, there is no suggestion or motivation to provide the claimed kits in view of the lack of suggestion that the dideoxynucleotides with attached linker and dye would function properly in sequencing. Therefore, Applicant submits that the present claims are properly patentable over the cited references, and requests that the Examiner reconsider and withdraw these rejections.

Applicant hereby requests a three-month extension of time to allow timely response up to and including September 9, 2002. A check for the fee for that extension is attached. No additional fee is believed due in connection with this Communication. However, if any additional fee is due, kindly charge the appropriate amount to Deposit Account No. 50-0872.

Respectfully submitted,

Date 9/8/2002
FOLEY & LARDNER
P.O. Box 80278
San Diego, CA 92138-0278
Telephone: (858) 847-6721
Facsimile: (858) 792-6773

By

Wesley B. Ames
Wesley B. Ames
Attorney for Applicant
Registration No. 40,893

Atty. Dkt. No. 026063-1402

Appendix 1 – Marked-up copies of amended claims

10. (Amended) A deoxyribonucleotide sequence containing a [the] compound of formula II, III, IV, or V.